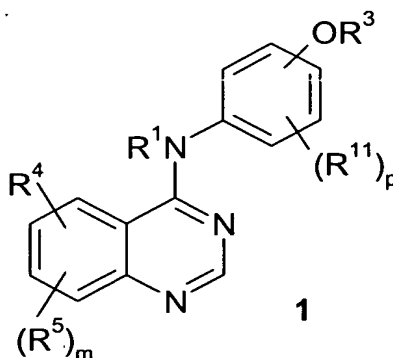


1. (Amended) A compound of the formula 1



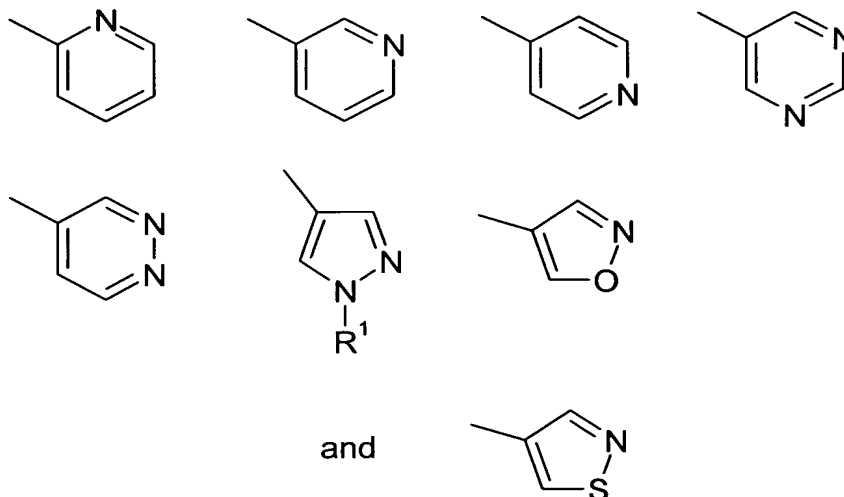
or a pharmaceutically acceptable salt, solvate or prodrug thereof, wherein:

m is an integer from 0 to 3;

p is an integer from 0 to 4;

each R¹ and R² is independently selected from H and C₁-C₆ alkyl;

R³ is selected from



wherein the foregoing R³ groups are optionally substituted by 1 to 3 R⁸ groups;

R⁴ is $-(CR^{16}R^{17})_m-C\equiv C-(CR^{16}R^{17})_tR^9$, $-(CR^{16}R^{17})_m-C\equiv C-(CR^{16}R^{17})_tR^9$, $-(CR^{16}R^{17})_m-C\equiv C-(CR^{16}R^{17})_kR^{13}$, $-(CR^{16}R^{17})_m-C\equiv C-(CR^{16}R^{17})_kR^{13}$, or $-(CR^{16}R^{17})_tR^9$, wherein the attachment point to R⁹ is through a carbon atom of the R⁹ group, each k is an integer from 1 to 3, each t is an integer from 0 to 5, and each m is an integer from 0 to 3;

each R⁵ is independently selected from halo, hydroxy, $-NR^1R^2$, C₁-C₆ alkyl, trifluoromethyl, C₁-C₆ alkoxy, trifluoromethoxy, $-NR^6C(O)R^1$, $-C(O)NR^6R^7$, $-SO_2NR^6R^7$, $-NR^6C(O)NR^7R^1$, and $-NR^6C(O)OR^7$;

each R⁶, R^{6a} and R⁷ is independently selected from H, C₁-C₆ alkyl, $-(CR^1R^2)_t(C_6-C_{10}$ aryl), and $-(CR^1R^2)_t(4 \text{ to } 10 \text{ membered heterocyclic})$, wherein t is an integer from 0 to 5, 1 or

a' 2 ring carbon atoms of the heterocyclic group are optionally substituted with an oxo (=O) moiety, the alkyl, aryl and heterocyclic moieties of the foregoing R⁶ and R⁷ groups are optionally substituted with 1 to 3 substituents independently selected from halo, cyano, nitro, -NR¹R², trifluoromethyl, trifluoromethoxy, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, hydroxy, and C₁-C₆ alkoxy;

or R⁶ and R⁷, or R^{6a} and R⁷, when attached to the same nitrogen atom, can be taken together to form a 4 to 10 membered heterocyclic ring which may include 1 to 3 additional hetero moieties, in addition to the nitrogen to which said R⁶, R^{6a}, and R⁷ are attached, selected from N, N(R¹), O, and S, provided two O atoms, two S atoms or an O and S atom are not attached directly to each other;

each R⁸ is independently selected from oxo (=O), halo, cyano, nitro, trifluoromethoxy, trifluoromethyl, azido, hydroxy, C₁-C₆ alkoxy, C₁-C₁₀ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, -C(O)R⁶, -C(O)OR⁶, -OC(O)R⁶, -NR⁶C(O)R⁷, -NR⁶SO₂NR⁷R¹, -NR⁶C(O)NR¹R⁷, -NR⁶C(O)OR⁷, -C(O)NR⁶R⁷, -NR⁶R⁷, -NR⁶OR⁷, -SO₂NR⁶R⁷, -S(O)_j(C₁-C₆ alkyl) wherein j is an integer from 0 to 2, -(CR¹R²)_t(C₆-C₁₀ aryl), -(CR¹R²)_t(4 to 10 membered heterocyclic), -(CR¹R²)_qC(O)(CR¹R²)_t(C₆-C₁₀ aryl), -(CR¹R²)_qC(O)(CR¹R²)_t(4 to 10 membered heterocyclic), -(CR¹R²)_tO(CR¹R²)_q(C₆-C₁₀ aryl), -(CR¹R²)_tO(CR¹R²)_q(4 to 10 membered heterocyclic), -(CR¹R²)_qS(O)_j(CR¹R²)_t(C₆-C₁₀ aryl), and -(CR¹R²)_qS(O)_j(CR¹R²)_t(4 to 10 membered heterocyclic), wherein j is 0, 1 or 2, q and t are each independently an integer from 0 to 5, 1 or 2 ring carbon atoms of the heterocyclic moieties of the foregoing R⁸ groups are optionally substituted with an oxo (=O) moiety, and the alkyl, alkenyl, alkynyl, aryl and heterocyclic moieties of the foregoing R⁸ groups are optionally substituted with 1 to 3 substituents independently selected from halo, cyano, nitro, trifluoromethyl, trifluoromethoxy, azido, -OR⁶, -C(O)R⁶, -C(O)OR⁶, -OC(O)R⁶, -NR⁶C(O)R⁷, -C(O)NR⁶R⁷, -NR⁶R⁷, -NR⁶OR⁷, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, -(CR¹R²)_t(C₆-C₁₀ aryl), and -(CR¹R²)_t(4 to 10 membered heterocyclic), wherein t is an integer from 0 to 5;

R⁹ is a non-aromatic mono-cyclic ring, a fused or bridged bicyclic ring, or a spirocyclic ring, wherein said ring contains from 3 to 12 carbon atoms in which from 0 to 3 carbon atoms are optionally replaced with a hetero moiety independently selected from N, O, S(O)_j wherein j is an integer from 0 to 2, and -NR¹-, provided that two O atoms, two S(O)_j moieties, an O atom and a S(O)_j moiety, an N atom and an S atom, or an N atom and an O atom are not attached directly to each other within said ring, and wherein the carbon atoms of said ring are optionally substituted with 1 or 2 R⁸ groups;

each R^{11} is independently selected from the substituents provided in the definition of R^8 , except R^{11} is not oxo(=O);

a¹ R^{12} is R^6 , $-OR^6$, $-OC(O)R^6$, $-OC(O)NR^6R^7$, $-OCO_2R^6$, $-S(O)_jR^6$, $-S(O)_jNR^6R^7$, $-NR^6R^7$, $-NR^6C(O)R^7$, $-NR^6SO_2R^7$, $-NR^6C(O)NR^{6a}R^7$, $-NR^6SO_2NR^{6a}R^7$, $-NR^6CO_2R^7$, CN, $-C(O)R^6$, or halo, wherein j is an integer from 0 to 2;

R^{13} is $-NR^1R^{14}$ or $-OR^{14}$;

R^{14} is H, R^{15} , $-C(O)R^{15}$, $-SO_2R^{15}$, $-C(O)NR^{15}R^7$, $-SO_2NR^{15}R^7$, or $-CO_2R^{15}$;

R^{15} is R^{18} , $-(CR^1R^2)_t(C_6-C_{10} \text{ aryl})$, $-(CR^1R^2)_t(4 \text{ to } 10 \text{ membered heterocyclic})$, wherein t is an integer from 0 to 5, 1 or 2 ring carbon atoms of the heterocyclic group are optionally substituted with an oxo (=O) moiety, and the aryl and heterocyclic moieties of the foregoing R^{15} groups are optionally substituted with 1 to 3 R^8 substituents;

each R^{16} and R^{17} is independently selected from H, C_1-C_6 alkyl, and $-CH_2OH$, or R^{16} and R^{17} are taken together as $-CH_2CH_2-$ or $-CH_2CH_2CH_2-$;

R^{18} is C_1-C_6 alkyl wherein each carbon not bound to a N or O atom, or to $S(O)_j$, wherein j is an integer from 0 to 2, is optionally substituted with R^{12} ;

and wherein any of the above-mentioned substituents comprising a CH_3 (methyl), CH_2 (methylene), or CH (methine) group, which is not attached to a halogeno, SO or SO_2 group or to a N, O or S atom, is optionally substituted with a group selected from hydroxy, halo, C_1-C_4 alkyl, C_1-C_4 alkoxy and $-NR^1R^2$.

The above amendments add no new matter to this application. Applicants respectfully request their entry.

REMARKS

Claims 1 to 21 are pending in the subject application. Applicants have hereinabove amended claim 1 and cancelled claims 2, 3 and 17 to 20 without prejudice to their right to pursue the cancelled subject matter in a later filed divisional or continuational application. Entry of this Amendment and reconsideration of the application as amended are respectfully requested. Upon entry of this Amendment claims 1, 4 to 16 and 21 are pending.

Applicants have provided after the signed page of this response a section entitled "VERSION WITH MARKINGS TO SHOW CHANGES MADE – DO NOT ENTER" to show the changes made to the claims of the subject application as required under 37 C.F.R. §1.121. Applicants respectfully submit that the amendment of the claims of the subject matter does